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EXAMINER	
MORAN, MARJORIE A	

ART UNIT	PAPER NUMBER
1631	25

DATE MAILED: 01/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/267,199	BHAT ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-18 and 20-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-18 and 20-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

In view of the new grounds of rejection set forth below, PROSECUTION IS HEREBY REOPENED. An office action on the merits of pending claims 10-18 and 20-25 is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

All rejections and objections not repeated below are hereby withdrawn.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See e.g. p. 16. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

35 U.S.C. 101/112 Utility Rejections

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 10-18, 20-22, and 24-26 are again rejected, as previously set forth and maintained in the office actions of 6/5/01 and 4/10/02, under 35 U.S.C. 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or by a well established utility.

Applicant's arguments filed in the Appeal Brief of 10/10/02 have been fully considered but they are not persuasive.

In response to the argument that the claimed nucleic acids are useful for determining the presence or absence of polymorphisms, or for acting as hybridization probes, in gene mapping, for isolation of homologous sequences, detection of gene expression, as molecular weight markers, and for "numerous other genetic engineering uses", the examiner maintains that these are general uses (purposes) applicable to the general class of nucleic acids and are not specific to the SEQ ID NO's claimed. It is well known in the art that polynucleotides, including others than those recited in the instant claims, can be used in hybridization assays to obtain other (e.g. homologous or complementary) nucleic acid sequences, to identify polymorphisms, etc. A nucleic acid molecule may have utility based on its use as a marker or probe for or related to a specific disease condition (e.g. probes for Huntington's chorea, cystic fibrosis, etc.); however, no correlation between a claimed SEQ ID NO: and a specific disease condition is taught by the instant specification. Similarly, a "use" for gene mapping or a chromosome "walk" requires that a correlation between a claimed nucleic acid sequence and a particular gene or chromosome be known. No correlation between an inventive sequence and a gene or chromosome is disclosed by the instant specification. A "use" to map a particular nucleic acid to a gene or chromosome is considered a "use" to do further research. A use as a marker is a generic use, and is not specific to any of the claimed sequences. A "use" for expression profiling requires knowledge of a time (e.g. developmental stage) and/or "place" (e.g. tissue) of expression, and knowledge of what a normal or abnormal level of expression is for the claimed nucleic acid. In the absence of such knowledge, the "use" of the claimed nucleic acid would be that of further research; i.e. to obtain information regarding expression (or lack thereof) in particular tissues and/or specific developmental stages. Applicant is reminded that a "use" to do further research is not a specific, substantial and credible utility under 35 USC 101. Isolation of a homologous sequence, wherein a utility for either the homologous sequence or the isolating sequence is not known, does not confer utility on the isolating sequence. Applicant equates use of his sequences to use of monoclonal antibodies for isolation of cells in flow sorting; however, it is

noted that antibodies, in general, have utility under 35 USC 101 due to their unique properties (in recognizing/binding to specific epitopes). Nucleic acids, in general, do not have utility based on recognized unique properties, therefore the comparison is not persuasive. Applicants further argue that as their nucleic acids encode enzymes of the tocopherol pathway, they can be used to modulate the tocopherol content and/or vitamin E content of plant tissues. In response, it is noted that the specification does not disclose that any of the claimed nucleic acid sequences is actually known to encode an enzyme of the tocopherol pathway, as set forth below. Further, it is not known or disclosed whether any of the claimed nucleic acid sequences is known to be involved in *modulation* of tocopherol or vitamin E synthesis.

In the instant case, it is asserted that the claimed nucleic acid molecules encode tocopherol synthesis pathway enzymes or fragments thereof. Each nucleic acid molecule claimed has at least one (and in most cases, several) ATG "codons". However, it is not known for ANY of the claimed sequences what the ORF is, therefore it is unknown whether any sequence is actually translated into a peptide, or, if translated, what the activity or function of that peptide may be. For example, SEQ ID NO: 161 comprises six "ATG' codons, but it is not known which, if any, is the start codon for a tocopherol synthesis pathway enzyme. Page 241 of the specification discloses that a putative peptide encoded by SEQ ID NO: 161 is 69% identical to a shikimate kinase enzyme from yeast, but there is no disclosure or evidence anywhere that the peptide so encoded has kinase activity, specifically shikimate kinase activity, or would be expected to have kinase activity (e.g. based on comparison of tertiary structures, active regions, conserved domains, etc.) It is possible that SEQ ID NO: 161 encodes a fragment of a shikimate kinase; however, it is not disclosed whether that fragment has activity or another function that the fragment has utility under 35 USC 101.

As previously set forth, homology alone is not evidence that a particular protein is indeed encoded by a recited nucleic acid sequence. See p. 7 of the office action of 11/21/00 regarding lack of predictability based on sequence homology. The prior art does not teach that the elected SEQ ID's encode the alleged proteins and the specification does not show that the peptides putatively encoded by the claimed nucleic acid sequences have an activity or function similar to those to which they are homologous.

As the instant specification does not disclose, and the prior art does not teach, that the instantly claimed nucleic acid sequences actually encode any protein or peptide, specifically the enzymes recited in Table A, the nucleic acid sequences represented by SEQ ID NO's 1, 100,

147, 153, 158, 161, 180, 199, and 232 do not have utility based on utility of a protein encoded thereby.

For all of the reasons previously set forth and set forth above, the rejections of claims 2,10-18, and 20-22 is maintained and new claims 24-26 are rejected.

Claims 10-18, 20-22, and 24-26 are also rejected under 35 U.S.C. 112, first paragraph for not being enabled.

Applicant's arguments have been fully considered but they are not persuasive. This enablement rejection is linked to the utility rejection, as previously set forth. As the utility rejection is maintained, the enablement rejection is also maintained.

Claim Rejections - 35 USC § 112, 1rst paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-18 and 20-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a LACK OF WRITTEN DESCRIPTION rejection.

The specification discloses SEQ ID NO's 1, 100, 147, 153, 158, 161, 180, 199, and 232. The specific sequences consisting of SEQ ID NO's 1, 100, 147, 153, 158, 161, 180, 199, and 232 meet the written description provisions of 35 USC 112, first paragraph. However, claims 10-22 and 24 recite open claim language (i.e. comprising, comprises, or having); claims 10-11, 13-15, and 17-21 specifically recite "fragments", and are also directed to encompass sequences which hybridize to SEQ ID NO's 1, 100, 147, 153, 158, 161, 180, 199, and 232. Claims reciting open claim language are also directed to encompass gene sequences, sequences that hybridize, corresponding sequences from other species, derivatives, allelic

variants, splice variants, and so forth. None of these sequences meet the written description provision of 35 USC 112, first paragraph. For example, a larger genetic sequence comprising introns, noncoding regions, etc., may comprise a claimed sequence or a "fragment thereof", or may hybridize to a claimed sequence, but be very different in overall sequence, structure, and function than the claimed SEQ ID NO: itself (i.e. the larger genetic sequence may encode entirely different proteins than those disclosed as putatively encoded by the claimed sequences). A sequence which hybridizes to the claimed sequences may have large portions which "bubble out" yet have sufficient similarity in sections to anneal under the claimed conditions. The specification provides insufficient written description to support the genus encompassed by the claims. Applicants argue that the claimed nucleic acid sequences/structures are described by the specification; this is not in dispute. It is noted that claim 25, which recites an isolated nucleic acid consisting of SEQ ID NO: 1, 100, 147, 153, 158, 161, 180, 184, 199, or 232 is not rejected herein. Applicant further argues, in summary, that the claims may be broader than a specific embodiment disclosed, that the specification need not particularly describe every embodiment encompassed by a claim, and that the specification does describe possible variants of the claimed SEQ ID NO's and that common structural features have been described for the claimed nucleic acids. In response, it is noted that while the claims may indeed be broader than specific embodiments disclosed in the specification, the description must still be sufficient to permit one skilled in the art to immediately envisage the product claimed. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species). In the instant case, the claims encompass sequences comprising introns, noncoding regions, and regions which do not hybridize to the claimed sequences, but which may still meet the claimed limitations, as set forth above. These sequences are not described by the instant specification and one skilled in the art would not be able to immediately envisage these products or structures.

With regard to claims 23-24, the specification discloses on pages 2-11 that the various enzymes recited in the claims are known and have been isolated from various sources; however, the specification does not disclose that SEQ ID NO: 158 is known to encode a maize shikimate dehydrogenase. The prior art teaches the gene encoding a maize shikimate dehydrogenase has been isolated (WENDEL et al. Biochem. Genetics (1988), vol. 26, pp. 421-

446), however, the sequences (alleles) taught by WENDEL are not recited in the instant specification nor is WENDEL incorporated by reference. No amino acid sequences are taught in the instant specification, nor is there any disclosure of a shikimate dehydrogenase, by structure or sequence, specific to maize. There is no disclosure that SEQ ID NO: 158 is known to actually encode a shikimate dehydrogenase, nor that SEQ ID NO: 158 is the same as or similar to the gene sequences isolated by WENDEL, nor that SEQ I DNO: 158 cosegregates with WENDEL's Sad1. SEQ ID NO: 158 comprises several possible start codons, and thus may putatively encode several peptide sequences. However, both a start and a stop codon in the same reading frame (e.g. an ORF) are necessary for proper translation into a functional protein or enzyme. No ORF is disclosed for SEQ ID NO: 158 which would indicate that applicant was indeed in possession of a sequence known to encode any peptide, specifically a shikimate dehydrogenase. For these reasons and those previously set forth, the rejection is maintained.

Claim 24 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an ENABLEMENT rejection.

Applicant's arguments filed with the Appeal Brief of 10/10/02 have been fully considered but they are not persuasive. In response to applicant's argument the specification (at Table A) discloses that SEQ ID NO: 158 exhibits 69% identity to a nucleic acid known to encode a maize shikimate dehydrogenase, it is noted that GI535771 is a nucleic acid encoding a shikimate dehydrogenase is tobacco, not maize (see NCBI accession no. AAA34069). As previously set forth, while the prior art teaches isolated nucleic acid sequences which encode a corn shikimate dehydrogenase, there is no evidence that the nucleic acids taught by the prior art are the same as those recited in the instant claims. Applicant admits on page 22 of the Appeal Brief that the examiner has presented art supporting the "general controversy in the art over prediction of function based on homology", then argues that the examiner has presented no evidence why one of ordinary skill in the art would reasonably doubt that a nucleic acid comprising SEQ ID NO: 158 would encode a shikimate dehydrogenase or fragment thereof. Given the admission that there is uncertainty in the art for predicting function based on sequence homology alone, and the lack of evidence or guidance in the specification for how to determine whether ANY peptide is actually encoded by and can be successfully translated from SEQ ID NO: 158, the

examiner maintains that it would require undue experimentation to determine whether SEQ ID NO: 158 encodes a shikimate dehydrogenase. Applicant argues that Example 4 sets forth parameters and a database for generating homology data; however, this is merely guidance for determining "hits'" in a Monsanto database. Example 4 provides no description for determining if a "hit" actually encodes the protein in the database. As previously set forth, SEQ ID NO: 158 comprises several putative start codons; however, for a peptide to be accurately translated, a stop codon in the correct reading frame must also be present. A "hit" indicating homology to a random nucleic acid sequence, with no knowledge of whether an ORF is present, is not a disclosure that a peptide can actually be translated from SEQ ID NO: 158. Further, the general parameters indicated in Example 4 do not indicate which "start" codon is indicated nor the bounds of the (possible) ORF, such that one skilled in the art would be able to determine which portion of SEQ ID NO: 158 was (or should be) used to generate the "hit" in Monsanto's database. The instant specification does not disclose any amino acid sequences which would allow one skilled in the art to determine which portion of SEQ ID NO: 158 would be expected to translate into a shikimate dehydrogenase or fragment thereof. Applicants argue that the specification provides evidence of sequence identity, discloses start and stop codons within a sequence, and discusses use of the claimed SEQ ID NO: to isolate additional sequences within a genome. As repeatedly set forth above, the specification does NOT identify start and stop codons within SEQ ID NO: 158. The sequence identity disclosed is to a tobacco protein, and given the degree of uncertainty in the art, does not persuasively show that SEQ ID NO: 158 actually encodes a protein with similar activity. Whether the claimed sequence can be used to isolate other sequences in a genome is not germane to whether the claimed sequence encodes a particular enzyme. As no information which would allow one skilled in the art to determine how to generate the specific peptides used for the homology comparisons of Table A of the instant specification are disclosed, the examiner maintains that it would require undue experimentation for one skilled in the art to determine how to generate a shikimate dehydrogenase from SEQ ID NO: 158.

In response to the arguments that practitioners attempting to determine whether the activity of a protein or peptide produced from SEQ ID NO: 158 is a shikimate kinase would be "guided by the high level of skill in the art and the present disclosure", it is noted that page 128 of the instant specification, to which applicant points, is directed only to general assays to detect transient gene expression in infected cells. There is no description anywhere in the instant

specification for detection of shikimate kinase activity. AS previously set forth, an assay to detect tyrosine kinase activity (e.g. as known in the art) would not necessarily detect shikimate kinase activity, therefore one skilled in the art would have to develop an assay to determine if a kinase with the claimed functionality and specificity (e.g. a shikimate kinase as opposed to a tyrosine kinase) were indeed produced. Also as previously set forth, the level of skill in the art is acknowledged to be high. An isolate nucleic acid encoding a maize shikimate kinase is known in the art (see below); however, the specification does not disclose if SEQ ID NO: 158 is the same as that taught by the prior art. One skilled in the art would therefore (a) have to determine which portion of SEQ ID NO: 158, if any, is an ORF possibly encoding a peptide, (b) determine if the protein produced is a shikimate kinase (e.g. determine if the homology "matches" that disclosed or taught by the prior art), and/or (c) determine whether the protein produced is an enzyme with the functionality and specificity recited in the claims. As the one skilled in the art must "guess" at some information (e.g. open reading frames, actual start codon, homology parameters) and/or develop new assays to arrive at the claimed invention, the examiner maintains that it would require undue experimentation for one skilled in the art to know how to make and use the claimed invention. For these reasons and those previously set forth, the rejection of claim 24 is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by SASAKI (NCBI accession number D23883, first seen 1129/1993), as supported by MEIKOTH et al. (Analyt. Biochem. (1984) vol. 138, pp. 267-284).

SASAKI teaches a sequence which is 52.9% identical to instant SEQ ID NO: 161. Using MEINKOTH's equation (Tm=81.5°C + 16.6 logM +0.41 (%G+C) - 500/n), taught on page 269, the melting point for a duplex between SEQ ID NO: 161 and SASAKI's sequence at 0.33 M salt (applicant's 2X SSC) would be 85.2°C. It is noted that applicant does not use formamide, therefore this term would be zero. Further, the length of the duplex (n) is 143 basepairs, therefore there is no correction (subtraction) for mismatches in the above calculation. If mismatches were subtracted, the melting point would be 84°C. A melting point of over 65°C indicates that SASAKI's sequence would inherently hybridize to a complement of instant SEQ ID NO: 161 under the claimed conditions, therefore claim 10 is anticipated.

Claim 23 is rejected under 35 U.S.C. 102(b) as being anticipated by WENDEL et al. (Biochem. Genetics (1988) vol. 26, pp. 421-446).

WENDEL teaches isolation of genetic alleles encoding shikimate dehydrogenase in maize (abstract), thereby anticipating claim 23.

Conclusion

Claims 10-18 and 20-26 are rejected; the specification is objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to an LIE, Tina Plunkett, whose telephone number is (703) 305-3524.

December 30, 2002

MARJORIE MORAN
PATENT EXAMINER

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